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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,002	12/27/2000	Martin Billger	01677710436	8872

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,002	BILLGER ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 17-36* is/are pending in the application.

4a) Of the above claim(s) *29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,17-28 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

I. Status of Application, Amendments, and/or Claims

The amendment filed in Paper No. 11 on January 10, 2003 has been entered in full. Claims 13-16 have been cancelled. Claims 1, 8, 9, 17, and 18 have been amended. Claims 19-36 have been added. Claims 1-12 and 17-36 are pending. Claims 1-12, 17-28, and 31-36 are under consideration and claims 29 and 30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a distinct invention from the one being examined (due to lack of unity of the invention).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

II. Withdrawn Rejections

The rejection of claims 1-3, 6-8, 10, 11, 13, 14, 17, and 18 under 35 U.S.C. §112, 2nd paragraph, as set forth at page 2 of the previous Office Action (Paper No. 8, September 10, 2002), has been withdrawn in view of applicants' amendment to the claims and cancellation of claims 13 and 14.

The rejection of claims 15 and 16 under 35 U.S.C. § 101 and 112, 2nd paragraph, as set forth at pages 2-3 of the previous Office Action (Paper No. 8, September 10, 2002), has been withdrawn in view of applicants' cancellation of the claims.

The rejection of claims 13-18 under 35 U.S.C. §112, 1st paragraph (enablement), as set forth at page 3 of the previous Office Action (Paper No. 8, September 10, 2002), has been withdrawn in view of applicants' amendment to claims 17 and 18 and cancellation of claims 13-16.

The rejection of claims 1-8 and 10-18 under 35 U.S.C. §102 (b), as set forth at page 4 of the previous Office Action (Paper No. 8, September 10, 2002), has been withdrawn in view of applicants' amendment to the claims.

III. Claim Rejections Under 35 U. S. C. § 103

(i) The rejection of claims 8 and 9 under 35 U. S. C. § 103 (a) as being unpatentable over Holthuis et al. (U.S. Patent 5,496,801, March 5, 1996) in view of Endo et al. (U.S. Patent 5,563,122, October 8, 1996) remains. The basis for this rejection is set forth at page 5 of the previous Office Action (Paper No. 8, September 10, 2002).

Applicants argue (i) that the prior art, as it related to the incorporation of sodium chloride in PTH formulations, is inconsistent at the time the present invention was filed; (ii) Holthuis et al. do not teach the impact of sodium chloride on PTH stability; (iii) Endo et al. require that sodium chloride be used in conjunction with a sugar to improve stability of PTH, but the present invention avoids sugars.

This has been fully considered but is not deemed to be persuasive for the following reasons, as well as for the reasons set forth in the previous office action (Paper No. 8, September 10, 2002).

First, while the Canadian patient CA 2,234,724 may teach a formulation preferably free of chloride ions, the majority of the art teach the use of saline (the aqueous solution of sodium chloride) as a water-based vehicle and the use of mannitol as an excipient in a formulation comprising human parathyroid hormone (see, e.g., column 1, U.S. Patent 5,496,801, March 5, 1996).

Secondly, despite that Holthuis et al. do not explicitly teach the impact of sodium chloride on PTH stability, Endo et al. clearly demonstrate that addition of sodium chloride, in addition to mannitol, further stabilizes PTH (See, e.g., Table 2).

Finally, since the claims use an open language, "comprising", it does not avoid the use of the sugars in the formulation, such as lactose and maltose, as applicants have argued; most importantly, Endo et al. teach that mannitol is the most preferred monosaccharide (top of column 2) and demonstrate clearly the combined effect of sodium chloride and mannitol on stabilizing PTH (Examples). Since the instant claims recite a pharmaceutical formulation comprising human parathyroid hormone, mannitol, and sodium chloride, the combination of the teaching of Holthuis et al. with that of Endo et al. clearly reads on the claims.

(ii) Claims 1-7, 10-12, 17-18, 21-23, 26-28, and 31-36 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Holthuis et al. (U.S. Patent 5,496,801, March 5, 1996) in view of Endo et al. (U.S. Patent 5,563,122, October 8, 1996).

Holthuis et al. teach a pharmaceutical formulation comprising human parathyroid hormone (1-84), mannitol as excipient, and citrate as buffering agent in

both liquid form and lyophilised form and a method for treating a bone related disorder, osteoporosis using the formulation (See, Abstract; 3rd paragraph of column 4). Holthuis et al. tech, for example, a formulation comprising human PTH (1-84) at 0.09 mg/ml to 2.27 mg/ml, 50 mg/ml mannitol, 10 mM citrate buffer at a pH between 4 and 6 (column 6). Holthuis et al. further teach that the recombinant form of the full length human hormone (1-84) is equipotent in studies on rats and shows in some respects somewhat improved efficacy in bone growth (3rd paragraph of column 1).

Holthuis et al. fail to teach inclusion of sodium chloride in their pharmaceutical formulation.

Endo et al. teach that addition of sodium chloride, in addition to mannitol, further stabilizes PTH (See, e.g., Table 2). Endo et al. teach that mannitol is the most preferred monosaccharide (top of column 2) and demonstrate clearly the combined effect of sodium chloride and mannitol on stabilizing PTH (Examples). Endo et al. further teach that the amount of sodium chloride to be added preferably from about 1/100-1/10 weight part of sugar (3rd paragraph of column 2). Thus, assuming the formulation of Holthuis et al. comprises 50 mg/ml mannitol, 0.5 mg/ml-5 mg/ml of sodium chloride would be needed according the teaching of Endo et al. In fact, Endo et al teach a formulation comprising 2mg/ml sodium chloride and 20 mg/ml mannitorl (See Example 3).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include sodium chloride in the formulation of Holthuis et al. with a reasonable expectation of success. One would have been

motivated to do so because Endo et al. demonstrate that addition of sodium chloride, in addition to mannitol, further stabilizes PTH (See, e.g., Table 2).

(iii) Claims 19, 20, 24, and 25 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Holthuis et al. (U.S. Patent 5,496,801, March 5, 1996) in view of Endo et al. (U.S. Patent 5,563,122, October 8, 1996), as applied to claims 1-12, 17-18, 21-23, 26-28, and 31-36 above, further in view of Selsted (U.S. Patent 5,547,939, August 20, 1996).

Holthuis et al. and Endo et al. teach pharmaceutical formulations and methods of treating a bone related disorder, e.g., osteoporosis, with the formulations as applied to claims 1-12, 17-18, 21-23, 26-28, and 31-36 above (i and ii).

Neither Holthuis et al. nor endo teach including a preservative (e.g., EDTA) in their pharmaceutical formulation.

Selsted teaches methods of inhibiting survival or growth of a microorganism using a composition comprising EDTA, which disrupts microbial membranes (1st paragraph of column 7).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further include a preservative, e.g., EDTA, in the formulations taught by Holthuis et al. in combination with Endo et al. with a reasonable expectation of success. One would have been motivated to do so because Selsted teach that EDTA disrupts microbial membranes and thus inhibits survival or growth of a microorganism.

IV. Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
March 14, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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